LETTERS TO THE EDITOR

Myocardial Metabolism of Hypertrophic Cardiomyopathy and Glucose Uptake

The recent article by Grover-McKay et al. (1) makes very interesting observations on the myocardial metabolism of hypertrophic cardiomyopathy. However, it also raises some concerns over the significance of glucose uptake in fasting subjects as imaged by positron emission tomography (PET). According to the study protocol, patients were requested to fast overnight with PET scanning the following day. Figure 1 demonstrates homogeneous N-13 ammonia uptake throughout the myocardium but abnormal F-18 2-deoxyglucose uptake in the septum relative to the lateral wall. The authors characterize this study as showing normal F-18 2-deoxyglucose metabolism in the lateral wall and abnormal F-18 2-deoxyglucose metabolism in the septum. Such analysis of a fasting F-18 2-deoxyglucose study is at variance with much of the published literature.

Myocardial glucose utilization depends on a number of hormonal and metabolic factors. Fasting creates a metabolic situation favoring free fatty acid oxidation over carbohydrate oxidation (2). Normal myocardium in the fasting state, therefore, will extract relatively little glucose at rest. F-18 2-deoxyglucose mimics initial extraction of glucose and will also be taken up to a minimal degree by the myocardium at rest and in the fasting state (3,4). Conversely, in the nonfasted state, myocardial uptake of glucose, and therefore F-18 2-deoxyglucose, is increased and imaging of normal myocardium is possible. Furthermore, Marshall et al. (5) were able to differentiate normal from ischemic tissue in the nonfasting state. As Gould (6) points out in a recent editorial, fasting F-18 2-deoxyglucose studies are useful to detect ischemia because only ischemic tissue will take up F-18 2-deoxyglucose in the fasting state. In the nonfasting state, both ischemic and normal tissue can be visualized.

The patient in Figure 1 may have "normal" F-18 2-deoxyglucose uptake in the lateral wall for several reasons: 1) normal tissue in a nonfasting state, 2) ischemic tissue in a fasting state, 3) globally abnormal glucose metabolism compared with known ischemic and nonischemic models.

Do the authors believe that fasting and nonfasting glucose metabolism in hypertrophic cardiomyopathy is truly opposite to that seen in normal individuals, or were their patients not truly fasting?

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Reply

Joyce's letter addresses an issue that is important for studies of myocardial metabolism with positron emission tomography (PET) and for interpretation of images of metabolism. At issue is myocardial F-18 2-deoxyglucose uptake in patients after an overnight fast as shown in Figure 1 of our recent article. As pointed out by Joyce, and as amply documented by others, myocardial glucose utilization depends on many factors (1,2). Levels of circulating glucose in plasma are an important determinant, as demonstrated initially by Bing et al. (3) and subsequently confirmed by Carlsten et al. (4). The myocardial extraction of glucose was found to be a function of the glucose plasma levels. These studies also demonstrated that when plasma fatty acid levels are high, as they are in the fasted state, as much as 60% to 70% of the oxygen consumption could be accounted for by oxidation of fatty acids. Importantly, the same studies reported myocardial utilization of glucose in the fasted state, although at lower rates compared with those in the post-absorptive state. The fact that myocardium continues to utilize glucose in the fasted state explains the observation of myocardial F-18 2-deoxyglucose uptake in our patients studied with PET after an overnight fast. Therefore, uptake of F-18 2-deoxyglucose in the lateral wall of the patient shown in Figure 1 of our article is indeed consistent with normal myocardium, one of three possible explanations suggested by Joyce. However, this uptake *can* be consistent with the fasting state, which is different from Joyce's contention.

The images shown in our report depict only the relative distribution of glucose utilization in myocardium and provide no information about absolute rates of glucose utilization. As observed by us and by others (5–7), glucose utilization in the fasted state may decline to levels at which uptake of F-18 2-deoxyglucose in normal myocardium can no longer be visualized on the cross-sectional PET images. In patients with coronary artery disease during exercise-induced ischemia, our experience with F-18 2-deoxyglucose (8) is consistent with findings by other groups as well as with animal experimental observations (7,9,10) that suggest preferential glucose utilization in ischemic and postischemic myocardium. F-18 2-deoxyglucose may be elevated in ischemic myocardium relative to normal myocardium or relative to blood flow in the ischemic segment. The latter point argues against Joyce's second contention, that tracer uptake in the lateral wall represents ischemia. In addition, tissue clearance kinetics of C-11 palmitate were similar in the septum and the lateral wall. Had ischemia been present in the lateral wall, we would have expected a regional decrease in the tissue clearance rate of C-11 activity and a decline in the early clearance curve component as we reported previously (11,12).

0735-1097/89/$3.50